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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,012	02/01/2005	Joachim Moormann	3868-0160PUS1	7480

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EXAMINER	
PALENIK, JEFFREY T	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
07/16/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/523,012	MOORMANN ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8-11,13-16 and 18-22* is/are pending in the application.

4a) Of the above claim(s) *10,11,13-16,18,19,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,8,9 and 20* is/are rejected.

7)☒ Claim(s) *21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

STATUS OF APPLICATION

Receipt is acknowledged of Applicants' Request for Continued Examination (RCE), Amendments and Remarks filed, 8 May 2009 in the matter of Application N° 10/523,012. Said filings are entered on the record. The Examiner further acknowledges the following:

Claims 2 and 12 are newly cancelled. No new claims have been added.

Claims 1, 3-6, 8-11, 13-16 and 18-22 are pending of which claims 10, 11, 13-16, 18, 19 and 22 remain withdrawn from consideration.

Regarding those claims still under consideration, claims 1, 5 and 9, have been amended. Claim 1 has been amended to more narrowly recite that the continuously release modulator of nicotinic receptors consists of galanthamine and the pharmaceutically acceptable salts there of. Claim 5 has been narrowed with the removal of nicotine and its acceptable salts. Claim 9 has been amended to remove the verbiage "capable of being".

No new matter has been added.

Claims 1, 3-6, 8, 9 and 20 now represent all claims currently under consideration.

INFORMATION DISCLOSURE STATEMENT

No new Information Disclosure Statement (IDS) have been filed for consideration.

PERFECTION OF APPLICANTS' PRIORITY

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. The Examiner acknowledges the receipt of the

certified foreign translation for German Patent Application 102 35 556.8, filed 3 August 2002. As such, Applicant has perfected their priority requirement and priority is extended to the above noted filing date.

WITHDRAWN OBJECTIONS/REJECTIONS

Objection to the Specification

Applicants' remarks regarding both the Abstract and Title of the Invention render moot their objection. Thus, after fully considering Applicants' remarks, said objections have been **withdrawn**.

Rejection under 35 USC 112

Applicants' amendment removing the "capable of being" limitation from claim 9, renders moot the rejection to claims 9, under 35 USC 112, second paragraph. Thus, said rejection has been **withdrawn**.

Rejection under 35 USC 103(a)

Applicants' amendments and remarks, particularly those directed to claim 1, render moot the rejection to claims 1, 3-6, 8, 9, 20 and 21, under 35 USC 103(a), as being unpatentable over Biberman et al. combined with Plata-Salaman et al. Of particular note, Applicants' note regarding Biberman that the galanthamine, may be optionally added to the formulations and that the MAO inhibitor is required by said formulations. Since the

combined references no longer nor render obvious the instantly amended claims (i.e. dispensing galanthamine alone), said rejection now stands **withdrawn**.

CLAIM OBJECTIONS

Claim 21 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim is improper form since it depends from cancelled claim 2. Claim 21 is withdrawn from consideration at this time.

NEW REJECTIONS

In light of Applicants' amendments and remarks, as well as the above withdrawn rejections, the following rejection has been newly added:

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-6 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Plata-Salaman (US Pre-Grant Publication N° 2003/0060423) and Moormann (USPN 5,643,905).

The instantly amended claim 1 is directed to a composition "characterized" by (e.g. comprising; see MPEP §2111.03) of two administration forms: 1.) an administration form that continuously releases at least one modulator of nicotinic receptors selected from galanthamine or one of its salts, and 2.) an administration form which enables a rapid entry of galanthamine or one of its salts in to the Central Nervous System, wherein the second form is further limited to one of the following routes of administration: buccal (i.e. sublingual) solutions, spray solutions or drip solutions (claim 1). The dependent claim 3 further limits the continuous release administration form to transdermal therapeutic systems, subcutaneous implants or intramuscularly injectible preparations. Claim 4 further limits the composition of claim 3

such that the intramuscularly injectible preparation is a suspension of microcapsules containing the modulator(s). Claim 20 further limits claim 1 such that the two dosage forms are administered independently.

Regarding the forgoing limitations, the Plata-Salaman reference expressly teaches co-therapy compositions comprising a therapeutically effective amount of one or more acetylcholinesterase inhibitors ¶¶[0018] and [0071], such as galanthamine ¶¶[0055] and [0056]. The term "co-therapy," as defined in ¶[0033], refers to at least one compound of a general "formula I" being administered with at least one acetylcholinesterase inhibitor wherein said compound(s) and inhibitor(s) are administered simultaneously, sequentially, separately or in a single pharmaceutical formulation. Instances where dosing does not occur in a single formulation, the routes of administration may be varied and include: intramuscular, transdermal, subcutaneous, as well as being directly applied to the nervous system. Topical, intranasal administration of the active agent is also taught ¶[0076]. Unit dose forms such as tablets, pills, and capsules, each of which include immediate-, timed-, and sustained release formats, are taught ¶[0072]. Additional dosing systems and formats such as injected (e.g. parenteral) suspensions, metered liquid sprays, drops, ampoules, and autoinjector devices are taught [0072], each of whose design is capable of incorporating distribution nozzles.

Plata-Salaman does not teach galanthamine or any of its salts as being the sole medicament of either the immediate or continuous release formulations. Nor is the intended use of treating addictions using galanthamine expressly discussed. However, the teachings of Moormann cure these deficiencies.

Moormann expressly teaches using galanthamine and the pharmaceutically acceptable salts thereof for the treatment of an addictive craving such as nicotine dependence (Abstract). It is further expressly suggested that galanthamine may also be used to treat alcohol withdrawal (col. 2, lines 62-64). Regarding forms of administration with which galanthamine may be delivered, Moormann expressly teaches that continuous and controlled delivery methods include oral, transdermal and parenteral modes (Abstract). The term "parenteral" is further defined as including application forms which exclude the oral form, such as intramuscular and nasal forms of administration (col. 2, lines 1-8).

Though both continuous and immediate forms of administration are expressly taught, the teachings of Moormann are deficient regarding the combined, but separate administration of galanthamine.

However, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to have prepared a combined yet sequential administration form consisting of galanthamine or one of it salts as instantly claimed. The ordinarily skilled artisan would have been highly motivated to prepare the instantly claimed composition, particularly since galanthamine-based formulations are capable of being separately co-administered (e.g. sequentially) as both a continuous form and as an immediate oral or nasal solution form as clearly taught by Plata-Salaman. Further motivation is provided by Moormann who expressly discusses a method for treating nicotine dependence using galanthamine (claims 1-4).

Based on the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable high expectation of successfully producing simultaneously

administered separate dosage forms consisting of galanthamine for treating addiction. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, alone or in combination, especially in the absence of evidence to the contrary.

Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Plata-Salaman, with respect to claims 1, 3 and 4, as set forth above.

Claim 5 further limits the continuous release administration form to either release between 10 and 25 mg of galanthamine or a pharmaceutically acceptable salt of it, per day, whereas claim 6 further limits the quick entry administration form of the composition such that it contains 1 to 5 mg of galanthamine or a pharmaceutically acceptable salt of it.

Regarding the teachings of Plata-Salaman, paragraph [0070] further expressly teaches that galanthamine is administered in an amount in the range of about 2 to about 32 mg daily and more preferably from about 4 to about 24 mg once or twice daily. The paragraph further teaches that Reminyl®, which is the unit dose tablet form of galanthamine, may be administered in a 12 mg dose.

Though amounts of galanthamine are taught, which would encompass the total amount of drug administered by the combination of the co-administered dosage forms, as claimed by Applicants, it is not expressly taught how much galanthamine is formulated into either of the dosage types. Since the values and formats of each parameter with respect to the claimed composition are adjustable, it follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a

routine practice that would be obvious for a person of ordinary skill in the art to employ. For example, Plata-Salaman expressly discusses that multiple dosage types and routes may be employed to deliver a total of 2-32 mg of galanthamine daily ¶¶[0070] and [0072]. Thus, it would have been customary for an artisan of ordinary skill, to adjust the formulated amount of galanthamine administered continuously as well as rapidly (e.g. nasally) in the composition, particularly in view of ¶¶[0070] and [0072], in order to achieve the desired delivery format. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of any of these parameters would have been obvious at the time of Applicants' invention.

Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Samuels (USPN 2,906,265), with respect to claim 1 as set forth above.

Claim 8 recites that the administration format for the rapid entry form is a flexible plastic container having a capacity between 1-5 mL. Claim 9 further limits claim 8 such that said plastic container is provided with nozzles through which the solution can be sprayed or dripped intranasally.

The teachings of Plata-Salaman are discussed above. Though intranasal administration of liquid sprays and drops is expressly taught ¶[0070], the actual device which contains and delivers said formulation is not expressly discussed.

However, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to have used a flexible plastic container having a nozzle in order to intranasally deliver the instantly claimed galanthamine formulation. The

ordinarily skilled artisan would have been highly motivated to do so and reasonably would have expected success because such containers are extremely well-known in the prior art. Such is evidenced, for example, by the teachings of Samuels which are directed to nasal adaptor devices which comprise a nozzle and a base portion (col. 1, lines 50-53). The practiced device is preferably constructed from flexible plastic (col. 2, lines 33-34) and may function to either drip or spray the contained formulation into the nose (claims 1 and 4). The format and parameters of such devices (e.g. containment volume), while not expressly taught, are well within the purview of the skilled artisan to optimize. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of the rapid-release dosage container would have been obvious at the time of Applicants' invention.

All claims have been rejected; no claims are allowed.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published

applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615